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Environmental factors in the aetiology of AutoImmune Liver Disease

Submission date
29/07/2015

Recruitment status
No longer recruiting

Registration date
24/09/2015

Overall study status
Completed

Last Edited
22/04/2021

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Our immune system normally protects us by attacking bugs that cause infections. Occasionally a person's immune system starts to attack the body instead. In autoimmune liver diseases (AILDs) an overaggressive immune system attacks the liver, resulting in damage leading to liver failure and cirrhosis (severe liver scarring). The main AILDs are Primary Biliary Cirrhosis (PBC), Primary Sclerosing Cholangitis (PSC) and Autoimmune Hepatitis (AIH). All three are rare diseases. People who develop AILDs need treatment to dampen down the immune system; many need lifelong treatment and some eventually need liver transplantation. The AILDs are likely due to a combination of genetic factors and environmental triggers. Some evidence suggests that there are groups of people affected by PBC where the disease is more common than in the general population (disease clusters). This may suggest that environmental factors around these groups are linked to disease development or severity. The aim of this study is to find out whether there are AILD disease clusters and to identify the environmental factors potentially responsible for this.

Who can participate?
All adult patients with a diagnosis of Primary Biliary Cirrhosis (PBC), Primary Sclerosing Cholangitis (PSC) and Autoimmune Hepatitis (AIH) in Northern England, and adults of the same gender and similar age who are not affected by liver disease.

What does the study involve?
This study will gather information on all patients with AILD who live in the North of England and look for clusters of patients. All patients will be asked to complete a questionnaire about the environment around them. Areas around clusters will be examined to look for chemicals/factors that may be linked to the development or progression of disease. If chemicals are found we will look for them in people with and without AILDs using blood samples. We will store the information and samples safely, so that they can be used to answer questions about AILDs that may come up in future. We will also ask people for permission to contact them or their doctors in the future if there are new studies in which they might be interested in participating.

What are the possible benefits and risks of participating?
Patients may benefit from the opportunity to be involved in research but there will be no direct

effect on their clinical care. No changes to treatment will be made as a result of taking part in the study. There are minimal risks associated with taking part in the study. The blood test may cause slight discomfort.

Where is the study run from?
Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust (UK).

When is the study starting and how long is it expected to run for?
March 2015 to December 2017.

Who is funding the study?
The National Institute for Health Research (UK).

Who is the main contact?
Dr Jessica Dyson

Contact information

Type(s)
Scientific

Contact name
Dr Jessica Dyson

Contact details
University of Newcastle upon Tyne
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United Kingdom
NE2 4HH

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18777

Study information

Scientific Title
Environmental factors in the aetiology of AutoImmune Liver Disease (EAILD): a cross-sectional study

Acronym
EAILD

Study objectives
To address the hypothesis that there are AILD disease clusters and to identify, using toxicological approaches, the environmental factors potentially responsible for disease clustering.

More details can be found here: http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=18777

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cornwall-Plymouth NRES Committee South West, 16/02/2015, REC ref: 15/SW/0048

Study design
Non-randomised; Observational; Design type: Cross-sectional study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Hepatology; Subtopic: Hepatology; Disease: All Hepatology

Interventions
Blood tests will be taken from consenting participants in the study. A trained research nurse, doctor, health care assistant or phlebotomist will take the samples, often at the participant's local hospital. For participants in Newcastle, blood sampling may be performed at the same time as their routine clinical blood tests so the number of procedures will be the same (i.e., same number of needle punctures) but the number of tubes of blood taken will be greater. 'Best-friends' will also be asked to complete the environment questionnaire and donate blood (optional).

Environment Questionnaire: Questionnaire will be given to the participant at introduction to the study for them to complete (paper or electronic format). Assistance from one of the research team will be available if required.

Seeking Consent: This will done in clinic or by post and participants able to return their signed consent form using a stamp-addressed envelope.

Patient participants will be asked if they are happy to be contacted for further studies if they meet the criteria for a given study.

Intervention Type
Other

Primary outcome measure
This is an observational study so there is no 'outcome' measure as such. A comprehensive case-finding approach will be used to identify all cases of AILDs in Northern England by developing a comprehensive database. The primary outcome measure will be whether there are disease clusters of cases in time and space.

All participants will be asked to complete the environment questionnaire and donate blood at time of recruitment to the study. This will be the only time they provide samples. The environment questionnaire data will be analysed at a later time point in the study. The blood samples will be tested later in the study when a suitable number of samples have been collected. Statistical modelling will be conducted on the database to assess if:
1. Cases of disease occur together in time and space more than expected by chance
2. Are there clusters of around key points such as industrial waste sites

Secondary outcome measures
1. Using the disease clusters there will also be an assessment of any interaction between socio-economic status and age that leads to exposure.
2. Clusters will be mapped onto already available information e.g. changing industrial pollution through time, collieries, waste sites, metal levels/chemicals (Reference Range Study), iron works, British Geological Survey and satellite imagery. The exposure to pollution changes over people's lives as they move and we will be able to include this information.
3. All patient participants will be asked to complete a detailed environment questionnaire and a clinical summary sheet which will provide demographic information and details about their diagnosis of AILD. Participants will also be asked to provide 1 set of blood samples but can opt out of this if they prefer.
4. A 'best-friend' approach will be used to gather information about people who do not have AILD. The 'best-friends' will be asked to complete the environment questionnaire and donate blood (optional).
5. Participants with AILD may also be asked if we can test the environment around where they live (optional). Samples from areas of high and low disease prevalence of AILD (water, air, soil, vacuum cleaner dust) may be tested for potential chemicals and toxins which might relate to disease. Any chemicals identified can be put through tests that we already have that are known to cause liver damage.
6. Chemicals/toxins may be tested for in the blood of participants with AILD and people without AILD using the 'best-friend' approach.

Overall study start date
26/03/2015

Completion date
31/12/2017

Eligibility

Key inclusion criteria
1. All adult patients with a diagnosis of Primary Biliary Cirrhosis (PBC), Primary Sclerosing Cholangitis (PSC) and Autoimmune Hepatitis (AIH) in Northern England who are able to give informed consent
2. The small minority who cannot give informed consent are not otherwise different from the rest of the study population, so have the potential to benefit from study outputs without the need to participate
3. 'Best-friend' participants will be adults of the same gender and similar age to patient participants who are not affected by liver disease

Participant type(s)
Mixed

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Total final enrolment
2622

Key exclusion criteria
Patients aged under 16 years. The systems and safeguards of the study will be established in consenting adult patients

Date of first enrolment
26/03/2015

Date of final enrolment
31/12/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

University of Newcastle upon Tyne
Newcastle upon Tyne
United Kingdom
NE2 4HH

Study participating centre
Each hospital in the Northern Deanery has been invited to participate in the study. Other sites are in various stages of set up.
United Kingdom
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Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

Sponsor details
Claremont Wing
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
England
United Kingdom
NE1 4LP

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Rare Diseases Translational Research Collaboration; Grantcode(s): BH149219/PD0252

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		04/11/2020	22/04/2021	Yes	No
HRA research summary			28/06/2023	No	No